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Sustained Reductions in Drug Use and Depression Symptoms from Treatment for Drug Abuse in Methamphetamine-Dependent Gay and Bisexual Men

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ABSTRACT *Methamphetamine abusers often complain of feelings of depression that can complicate accurately diagnosing these individuals during treatments for methamphetamine abuse. This article presents an examination of temporal associations between documented methamphetamine use and reported ratings of depression among 162 gay and bisexual male methamphetamine abusers who participated in a 16-week randomized clinical trial of four behavioral therapies for methamphetamine abuse. Methamphetamine use was measured using thrice-weekly urine samples analyzed for drug metabolite. Self-reported depressive symptoms were collected weekly using the Beck Depression Inventory (BDI). At treatment entry, 73.2% of participants rated their depressive symptoms as mild or higher in severity (BDI≥10), with 28.5% reporting BDI scores in the moderate to severe range (BDI≥19). All participants reported significant decreases in depressive symptoms from baseline through the end of treatment, regardless of treatment condition, HIV status, or mood disorder diagnosis. A mixed regression model showed methamphetamine use for up to 5 days prior to the BDI score strongly predicted depressive symptoms ($F_{1, 968}=18.6$, $P<.0001$), while BDI scores had no significant association with subsequent methamphetamine use. Findings show that behavioral methamphetamine abuse treatment yields reductions in methamphetamine use and concomitant depressive symptom ratings that are sustained to 1 year after treatment entry.*

KEYWORDS *Depression, methamphetamine, drug abuse treatment, gay men.*

INTRODUCTION

Methamphetamine abusers frequently complain of depression. Indeed, symptoms of depression figure prominently in the methamphetamine withdrawal syndrome.[1,2] Depressive symptoms are noted during immediate withdrawal and during the initial weeks and sometimes months of abstinence following cessation of methamphetamine use.[3] Although it may be clinically important to identify co-occurring depressive disorders among treatment-seeking methamphetamine-abusing individuals, the task is

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difficult. Substance-induced mood disorder is used to denote individuals evaluated with significant depressive symptoms when there is evidence of recent methamphetamine use.[1] Only observation of the individual during protracted periods of abstinence from methamphetamine use allows confidence in a diagnosis of a primary mood disorder. Clinicians are often faced with the challenge of determining the relative amount of attention to devote toward co-occurring disorders during drug abuse treatment.

The clinical literature generally indicates that drug abuse treatments can affect methamphetamine use and alleviate ratings of depression. Kalechstein et al.[4] reported that 57.1% of methamphetamine-dependent prison and jail inmates reported depressive symptoms within the year prior to intake, but did not indicate whether depressive symptoms preceded onset of drug use or drug use associated with the emergence of depressive symptoms. Huber[5] reported that the behavioral drug abuse treatment of contingency management (provision of increasingly valuable reinforcers for consecutive urine samples that document methamphetamine abstinence) significantly reduced methamphetamine use, but had no effects on depression ratings (Beck Depression Inventory; BDI). This study tested sertraline compared with placebo and found significant medication effects on BDI ratings compared with placebo, although sertraline had no effects on methamphetamine use. Galloway et al.[6] found no significant effects for the antidepressant imipramine as a potential methamphetamine abuse treatment compared with placebo, either in reductions of methamphetamine use during treatment or of depression ratings. Finally, in a study that contacted individuals treated for methamphetamine abuse 2–5 years prior, significant reductions in methamphetamine abuse were reported by most participants. By contrast, self-reports of recent depressive symptoms were found in similar proportions at follow-up evaluations (62.7%) as at admission to treatment (62.9%).[7]

In the United States, methamphetamine use is common among gay and bisexual men, particularly in urban areas.[8] Gay and bisexual men are also three times as likely to meet criteria for current major depression as heterosexual men.[9] Although population-based studies indicate that any report of methamphetamine use by gay and bisexual men significantly associates with reported HIV infection,[10,11] the extent to which depressive symptoms may be mediated by both HIV infection and methamphetamine dependence in gay and bisexual men is unknown.

This article reports the prevalence and severity of depressive symptoms at baseline, weekly during treatment, and at 16, 26, and 52 weeks after behavioral drug abuse treatment among methamphetamine-dependent gay and bisexual men in Los Angeles. Analyses explored associations between HIV serostatus, formal depression diagnoses, and self-reported depressive symptoms. The temporal association between methamphetamine use and depression ratings during treatment was also tested. A higher rate of depressive disorders was predicted among HIV-seropositive participants than HIV-seronegative participants as well as a greater severity of depressive symptoms associated with methamphetamine use during treatment.

METHOD

Participants

Participants who met the following inclusion criteria were enrolled in a 16-week study: seeking treatment for their current methamphetamine use problem; diagnosed with methamphetamine dependence (verified by a Structured Clinical Interview for the DSM-IV[12]); self-identified gay or bisexual men; between the ages of 18 and 65

years; and willing to provide informed consent to participate in the treatment research study. The study was conducted in an outpatient treatment research clinic in the Hollywood and West Hollywood areas of Los Angeles from 1996 to 2001.

Procedure

The Friends Research Institute West Coast Institutional Review Board oversaw all research activities consistent with the Belmont Report. Potential participants met with a study investigator to receive an explanation of the potential risks and benefits to participation. Those willing to participate provided written informed consent. Study procedures are reviewed briefly here; for more details see Shoptaw et al.[13]

Following provision of written informed consent, 263 study participants began a 2-week baseline period that required completion of assessments to characterize the sample. The 162 participants completing the baseline period, including attending at least 2 of 4 "early recovery skills" groups, were randomly assigned to one of four treatment conditions. To provide multivariate balance of variables known to correlate with outcome, ethnicity and level of methamphetamine use were used as factors during an urn randomization procedure[14] when assigning participants to treatment conditions. Participants attended clinic three times per week for a treatment period of 16 weeks and were scheduled for follow-up visits at 26- and 52-weeks after randomization. Only participants who completed the baseline period and were randomized to the intensive outpatient behavioral treatment research were included in these analyses.

Measures

Admission Form This 8-page measure collects information describing participant demographics, drug use behaviors, drug and alcohol treatment history, sexual risk behaviors, and medical and psychiatric backgrounds. Additional questions included HIV serostatus at last testing.

Beck Depression Inventory The BDI[15] is a 21-item self-administered scale that is widely used for screening and diagnostic assessment of depression as well as for monitoring therapeutic progress. Mild depression was indicated by scores of 10–19, moderate depression was indicated by scores of 19–29, and BDI totals over 30 indicated severe depression. Individuals with BDI scores ≥15 or any responses indicating suicidal ideation were referred to a counselor to assess need for intervention. The BDI was administered weekly.

Structured Clinical Inventory for DSM-IV The Structured Clinical Inventory (SCID) for DSM-IV,[12] a semistructured clinical interview, was conducted by a trained clinician and used to assess current and historical DSM-IV (Diagnostic and Statistical Manual of Psychiatric Disorders—4th Edition) Axis I disorders such as mood and anxiety disorders. The only Axis II disorder assessed was antisocial personality disorder.

Assessment of Methamphetamine Use Recent methamphetamine use was assessed at each clinic visit (thrice weekly) by analyzing observed urine samples for the presence of metabolites of methamphetamine utilizing on-site SYVA EMIT Dade-Behring radioimmunoassay machine. Distal methamphetamine use was assessed at baseline and weeks 16, 26, and 52 using the 30-day self-report scores of the Addiction Severity Index.[16]

Interventions Participants were randomly assigned to one of four treatment conditions.

Cognitive Behavioral Therapy The Matrix Model of Cognitive Behavioral Therapy[17] used in this study adopted a framework that promotes a focus on maintenance of the habit change process. Thrice-weekly CBT groups focused on teaching patients to recognize "triggers" for their stimulant use, to develop healthier coping strategies for handling "triggers", and to minimize the extent of a relapse should one occur. On average, participants attended 40.8% of the 48 possible sessions.

Contingency Management Originally developed by Higgins and colleagues,[18] contingency management (CM) has been utilized in numerous applications of substance abuse treatment and is effective for increasing treatment retention and abstinence. CM procedures consisted of providing vouchers of increasing value for urine samples documenting continuous abstinence from methamphetamine. Over the 16-week period, participants had the potential to earn up to $1,277, although the average amount actually earned per participant in the condition was $415.

CBT+CM Participants assigned to this condition received the CM intervention and attended CBT groups. On average participants attended 73.8% of the total CBT sessions possible and earned $662 in vouchers.

Gay-Specific CBT The fourth condition consisted of a culturally relevant CBT that integrated the basic tenets of the Matrix Model CBT with culturally specific educational materials and exercises designed to reduce the frequency of HIV-related sexual risk behaviors. The manual-driven intervention contained 48 sessions delivered in thrice-weekly groups over 16 weeks. Participants in the Gay-specific CBT condition attended an average 55.8% of the total possible sessions.

Data Analysis

BDI total scores were compared between conditions at baseline and at weeks 16, 26 and 52 by using one-way analysis of covariances (ANCOVAs) (baseline covaried). The rate of change for BDI total scores between baseline and week 1 was assessed using a paired *t* test. Tests for differences in BDI total scores by HIV serostatus were conducted using analysis of variance (ANOVA). Differences in BDI total scores for participants with and without Axis I disorders were analyzed at baseline, weeks 16, 26 and 52 using *t* tests. A total of 7 SCID interviews were missing in all or part, leaving a final sample of 155 interviews upon which analyses of SCID and BDI total scores were tested. Missing data were handled using casewise deletion. All tests adopted an alpha level of $P<0.05$, two-tailed.

To examine the temporal association between methamphetamine use and reported depressive symptoms, a piecewise linear mixed regression model with random intercepts was developed in which the outcome variable (weekly BDI score after a logarithmic transformation) was regressed on thrice-weekly urine drug screening results. This type of analysis uses all available data at all time points and is less susceptible to biases from missing data. The predictor variable in this mixed model was the participants' results indicating detection or absence of detection of methamphetamine metabolite in urine drug screens. This model estimated the following: urine drug screen results 5 days prior to BDI score, 3 days prior to BDI

score, same day as BDI score, 3 days after BDI score, and 5 days after BDI score. The estimate reported represents the strength of association and the direction of association between these variables.

RESULTS

Demographic and drug use characteristics of the 162 self-identified gay and bisexual men enrolled in this outpatient treatment research program for methamphetamine dependence are presented in Table 1. Across all behavioral treatments, dramatic and significant reductions in recent self-reported methamphetamine use were observed from baseline (9.6 days; standard deviation, SD = 7.4) to week 16 (2.4 days, SD = 5.3), week 26 (2.2 days, SD = 4.8), and week 52 (3.6 days, SD = 6.4; $F_{3, 505} = 44.1$, $P < .0001$).

BDI total scores at baseline indicated at least mild depressive symptoms for most (73.2%) participants. Of 153 baseline BDI scores, 44 (28.5%) were in the moderate to severe range ($M_{BDI} = 25.0$, SD = 5.6); 69 (44.8%) were in the mild to moderate range ($M_{BDI} = 13.7$, SD = 2.3); and 41 (26.6%) in the no depression to minimal depression range ($M_{BDI} = 5.5$, SD = 2.7). More than one-half (52.9%) of participants met criteria for a lifetime mood disorder (SCID verified), with 28.4% of the sample meeting criteria for a lifetime major depressive disorder (MDD). No statistically significant differences in severity of reported depressive symptoms were

TABLE 1. Demographics, baseline drug use, and baseline sexual risk behaviors of 162 randomized participants

Variable	Mean (SD) or percentage
Mean age (years)	36.6 (6.4)
Education	
At least high school	95.7
At least 4-year degree	41
Ethnicity	
Caucasian	77.2
Hispanic	12.9
African American	3.1
Asian-American	3.1
Native American	1.2
Reported drug use behaviors	
Lifetime methamphetamine use (years)	8.34 (5.9)
Lifetime number of other illicit drugs used (number of drugs)	2.3 (1.4)
Any lifetime injection methamphetamine use	32.1
Methamphetamine use in past 30 days (days of use)	9.7 (7.4)
Dollars spent on methamphetamine past 30 days	$293 (339)
Sexual risk behaviors	
Sexual partners (number in past 30 days)	9.9 (20.9)
Sexual partners (number in past 6 months)	44.3 (78.3)
Had sex in public place (e.g., bathhouse) (in the past 30 days)	43.8
UAI with other than primary partner (in the past 30 days)	49.4
UAI that took place while using methamphetamine	83.8
HIV seropositive by self-report	60.5

UAI, unprotected anal intercourse.

found between treatment conditions at baseline, 16, or 26 weeks; instead, a general sustained reduction in depressive symptoms was observed (Figure). Most of the decrease took place in the first month ($M_{baseline} = 14.3$, $SD = 8.0$, $M_{week\ 4} = 6.8$, $SD = 6.8$; $t(111) = 9.4$, $P < .001$), with the largest drop in BDI scores occurring between baseline and the first week ($M_{baseline} = 14.8$, $SD = 8.2$, $M_{week\ 1} = 9.4$, $SD = 7.3$; $t(139) = 9.1$, $P < .001$). No statistically significant differences were found for BDI scores when analyzed by presence of diagnosis of MDD or of HIV serostatus.

At 52-week follow-up, participants in the CBT-only condition had higher BDI scores ($M_{CBT} = 10.3$, $SD = 7.8$) than participants in the other conditions ($M_{GCBT} = 6.6$, $SD = 6.2$; $M_{CM} = 5.7$, $SD = 6.7$; $M_{CBT+CM} = 4.6$, $SD = 5.6$; $f(3,120) = 3.9$, $P = .01$). *Post hoc* analysis revealed that participants in the CBT condition diagnosed with current MDD at baseline had significantly higher BDI scores than participants not diagnosed with current MDD at the follow-up visit ($M_{MDD} = 22.7$, $SD = 5.5$; $M_{non\text{-}MDD} = 7.9$, $SD = 5.9$; $t(20) = -4.0$, $P < .001$). As well, more of the CBT participants (38.6%) had a lifetime history of MDD at baseline than participants in any other condition (CM = 22.7%; CBT + CM = 25.0%; GCBT = 16.6% ($\chi^2(3) = 7.9$, $P < .05$).

Estimates of the temporal associations between thrice-weekly collected urine samples and the weekly depression ratings were significantly and positively associated. Samples documenting recent use of methamphetamine predicted future high BDI scores and samples documenting recent prior abstinence of methamphetamine predicted future low BDI scores [$f(1, 968) = 18.6$, $P < .0001$; Table (2)]. By contrast, BDI scores did not predict future methamphetamine use.

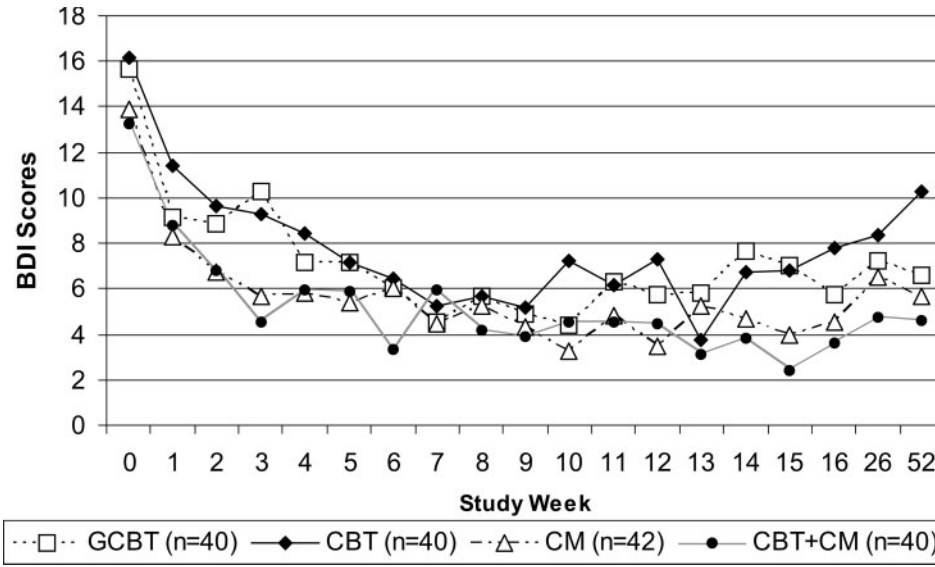

FIGURE. Average BDI scores by condition at baseline (week 0), during treatment (weeks 1–16) and at 26- and 52-week follow-up evaluations.

TABLE 2. Mixed model results evaluating estimates of the temporal association between Beck Depression Inventory scores (collected once per week) and urine drug screening results (collected three times per week)

	Time				
	−5 days	−3 days	Same day	+3 days	+5 days
BDI					
Urine*	0.1599	0.2117	0.4103	0.0565	0.0369
P†	.0099	.0004	.0001	.3650	.5607

*Values denote the estimate of the association between the weekly Beck Depression Inventory totals and the thrice-weekly urine samples using the mixed model.

†*P* values of the estimates of the temporal association between the Beck Depression Inventory totals and the urine samples.

DISCUSSION

These behavioral drug abuse treatments were effective in reducing self-reported methamphetamine use among participants through the one-year follow-up evaluations. The vast majority of participants reported at least mild depressive symptoms at baseline, likely reflecting the high prevalence of depressive symptoms associated with methamphetamine withdrawal.[1] These findings provide evidence of a strong association between methamphetamine use, co-occurring depressive disorders, and current depressive symptoms.[19] However, the hypothesis that HIV-seropositive men would exhibit higher levels of depressive disorders as well as current depressive symptoms than HIV-seronegative men was not supported.

Depression ratings improved equally across conditions from baseline through the 52-week follow-up evaluation, except that participants in the CBT-only condition reported significantly higher levels of depressive symptoms than participants in all other conditions at the 52-week point. This difference was likely due to a subgroup of participants in the CBT-only group who had a current MDD diagnosis at screening.

A reduction in both methamphetamine use and depressive symptoms for 52 weeks following treatment admission differs from previous findings. Huber et al.[5] reported reductions in methamphetamine use, but not depressive symptoms, at 2- to 5-year follow-up evaluations of heterosexuals receiving behavioral therapy for methamphetamine abuse. The different findings could stem from a number of factors, such as the multi-year evaluation period used by Huber et al.[5] or the Huber group's use of the Brief Symptom Inventory to measure depressive symptoms rather than the BDI. There may also be factors associated with sexual orientation or other characteristics among the participants that account for these divergent findings. Nonetheless, the results from this study are encouraging, particularly given that the largest reductions occurred within the first week. The immediate benefits observed in mood function corresponding to cessation of methamphetamine use may in part reflect structural effects of entering and engaging in treatment.

There was no evidence for the oft-heard claim that individuals use methamphetamine because they feel depressed. Instead, these data indicate that individuals felt

depressed due to recent methamphetamine use and less depressed when they had recently abstained. It is of interest that current ratings of depression had no predictive association with future methamphetamine use. Similar to abuse of nicotine and opioids, it is likely that a negative reinforcement process is operating such that methamphetamine use is experienced and remembered as a potent reliever of depressive symptoms, thus generating the drug user's perception that they use to feel less depressed.

These findings show sustained reductions in methamphetamine use and in depressive symptoms in a high-risk group for up to 1-year follow-up evaluations and suggest that the specific type of structured behavioral or cognitive-behavioral treatment may be of little consequence over the longer term. Data indicate that it is more important that individuals enter a structured treatment program where they are actively confronting and addressing their substance abuse. That all participants were required to attend treatment thrice-weekly for 16 weeks may have produced nonspecific structural effects. Future work might examine the efficacy of less intensive interventions to meet the needs of a more substantial proportion of gay and bisexual male methamphetamine users. As well, the costs of contingency management may be difficult for community agencies to adopt; less expensive contingency management strategies should be evaluated.

These outcomes are limited in that they are from a single trial conducted in one US city with a very specific population of methamphetamine users—urban treatment-seeking gay and bisexual men. Results may not hold true for other populations of methamphetamine users. Moreover, given ethical considerations, a no-treatment control condition was untenable. The relationship between methamphetamine use and depressive symptoms among gay or bisexual male methamphetamine users receiving no treatment was therefore not evaluated. Participants in this trial tended to be in their mid-30s and of Caucasian ethnicity. It is unknown whether these results would hold true for younger or older gay men, or for gay or bisexual men primarily of ethnic minority status. Nonetheless, the findings provide strong support for the potential of behavioral drug abuse treatments to achieve long-term reductions in depression, current depressive symptoms, and methamphetamine use among gay or bisexual male methamphetamine users.

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